UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF CHEMICAL SAFETY AND POLLUTION PREVENTION

OPP OFFICIAL RECORD
HEALTH EFFECTS DIVISION
SCIENTIFIC DATA REVIEWS
EPA SERIES 361

MEMORANDUM

Date: November 3, 2011

SUBJECT: Cyhalofop-butyl. Amended Tolerance Petition for use on Rice and Wild Rice. Summary of Analytical Chemistry and Residue Data

PC Code: 082583
Decision No.: 445028
Petition No.: 1F7836
Risk Assessment Type: NA
TXR No.: NA
MRID No.: 48031201

DP Barcode: D395669
Registration No.: 62719-357, 62719-613
Regulatory Action: Section 3
Case No.: NA
CAS No.: 122008-85-9
40 CFR: §180.576

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Executive Summary

Cyhalofop-butyl is a highly selective aryloxyphenoxypropionic herbicide registered to Dow AgroSciences, which was developed to control many annual and seedling perennial grasses, including barnyard grass (*Echinochloa crus-galli*) and sprangletop (*Leptochloa spp*) in rice. Cyhalofop-butyl acts through inhibition of the plant acetyl Coenzyme-A carboxylase, a pivotal enzyme in plant fatty acid biosynthesis.

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Dow AgroSciences has submitted an amended tolerance petition for the use of the herbicide cyhalofop-butyl (R-(+)-n-butyl-2-(4-(4-cyano-2-fluorophenoxy)-phenoxy)propionate) on rice and wild rice. Tolerances have been previously established for cyhalofop-butyl and its acid and diacid metabolites in/on rice grain and wild rice grain at 0.03 ppm (40CFR §180.576). Dow has requested that amended tolerances of 0.40 ppm be established for residues of cyhalofop-butyl and its acid and diacid metabolites in/on rice, grain and rice, wild, grain. These amended tolerances are required due to recently submitted side-by-side field trial data submitted to support a new formulation of cyhalofop-butyl (Memo, D380977, W. Drew, 9/24/2010).

The residue chemistry aspects of the use of cyhalofop-butyl on rice were discussed in detail in the residue chemistry review prepared for the previously reviewed petition for use of cyhalofop on rice (Memo, D267558, M. Nelson, 11/13/2001). This memo discusses all of the following topics: the nature of the residue in rice, the nature of the residue in ruminants and poultry, the residue analytical methods, storage stability of residues in rice commodities, water/fish/irrigated crops, field trial studies, rice processing data, residues in meat/milk/poultry/eggs, and confined and field accumulation in rotational crops. HED translated this information to wild rice under the previously reviewed petition for wild rice (Memo, D352156, D. Dotson, 7/7/2009).

In support of a petition for a new formulation of cyhalofop-butyl, Dow submitted a rice field trial study (MRID #48031201) to obtain side-by-side residue comparisons between a currently registered formulation (Clincher SF), and a new formulation (Clincher GR) of cyhalofop-butyl. The petition for this new formulation was previously reviewed and approved (Memo, D380977, W. Drew, 9/24/2010). Clincher GR (EPA File Symbol 62719-613), the new end-use product (EP) proposed for use on rice, is a granular (G) formulation containing 1.7% (by weight) of cyhalofop-butyl as the active ingredient (ai). Clincher SF (EPA Registration #62719-357), the currently registered EP, is an emulsifiable concentrate (EC) formulation containing 2.38 pounds of ai per gallon (lb ai/gal) of cyhalofop-butyl. Six field trials were conducted in EPA Regions 4, 6 and 10 (2 trials in each region). Target rates for both EPs were 0.28 lb ai per acre (lb ai/A) for the first application, and 0.19 lb ai/A for the second application, for a total of approximately 0.47 lb ai/A. This is the maximum seasonal use rate for cyhalofop-butyl. Applications of Clincher SF required the addition of an agriculturally approved crop oil concentrate. No adjuvant was used with Clincher GR applications. The first application of both formulations was made 15 to 34 days post-planting. The second application of both formulations was made at approximately 60 days prior to harvest.

The available storage stability data adequately support the sample storage durations and conditions incurred during the rice field trial study (D277192; M. Nelson; 13 November 2001). No storage stability corrections need to be applied to the rice field trial results.

Residues of cyhalofop-butyl (as cyhalofop acid), cyhalofop acid, and cyhalofop diacid in rice grain and straw were determined using liquid chromatography with tandem mass spectrometry detection (LC/MS/MS). The limit of detection (LOD), and limit of quantitation (LOQ) for the method were 0.003 ppm and 0.010 ppm, respectively.

The maximum combined residue (cyhalofop-butyl, cyhalofop acid, and cyhalofop diacid) in rice grain, resulting from application of Clincher GR at the maximum seasonal use rate (0.47 lb ai/A), was 0.015 ppm, while the minimum combined residue was non-detectable (ND). The mean combined residue was 0.004 ppm, with a standard deviation of 0.006 ppm. The highest average field trial (HAFT) residue was 0.015 ppm. This data was used to support the approval of the Clincher GR formulation, with the existing tolerances of 0.03 ppm being adequate to support anticipated residues.

However, unexpectedly high residues were observed in the field trials for Clincher SF, with a maximum combined residue in rice grain of 0.277 ppm, resulting from application of Clincher SF at the maximum seasonal use rate (0.47 lb ai/A), while the minimum combined residue was non-detectable (ND). The mean combined residue was 0.097 ppm, with a standard deviation of 0.125 ppm. The highest average field trial (HAFT) residue was 0.273 ppm. Residues arising from use of the G formulation, Clincher GR, were significantly lower in all harvested samples (collected 59 to 61 days after the last treatment) than those found after treatment with Clincher SF, an EC formulation.

Tolerances for residues of cyhalofop-butyl are listed under 40CFR §180.576[a]. Permanent tolerances are currently established for cyhalofop-butyl residues in/on the grains of rice and wild rice at 0.03 ppm. No tolerances are currently established for residues in animal commodities or in rotational crops and the conclusion that there is no expectation of finite residues in these commodities remains unchanged. Given the new residue data for Clincher SF, HED recommends in favor of the establishment of an amended tolerance of 0.40 ppm for rice, grain and rice, wild, grain. No Codex, Canadian, or Mexican MRLs have been established for cyhalofop-butyl. As a result, these amended tolerances will not create international MRL harmonization issues.

Regulatory Recommendations and Residue Chemistry Deficiencies

There are no residue chemistry deficiencies that would preclude the granting of amended tolerances for rice, grain and rice, wild, grain. The submitted data support the following amended tolerance for residues of cyhalofop-butyl and its acid and diacid metabolites in/on:

Rice, grain	0.40 ppm
Rice, wild, grain	0.40 ppm

The existing tolerances of 0.03 ppm on rice, grain and wild rice, grain should be replaced with these amended tolerances of 0.40 ppm given the recently submitted residue data.

Background

The chemical structure and nomenclature of cyhalofop-butyl are provided in Table 1, below. The physicochemical properties of the technical grade of cyhalofop-butyl are presented in Table 2.

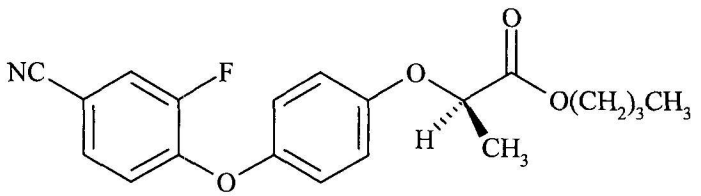
Table 1. Cyhalofop-butyl Nomenclature.	
Compound	
Common name	Cyhalofop-butyl
IUPAC name	2-(4-(4-cyano-2-fluorophenoxy)phenoxy)propanoic acid, butyl ester (R)
CAS name	R-(+)-n-butyl-2-(4-(4-cyano-2-fluorophenoxy)-phenoxy)propionate
CAS registry number	122008-85-9
End-use product (EPs) requested for registration	Clincher® CA Herbicide (29.6% Emulsifiable Concentrate)

TABLE 2 Physicochemical Properties of Cyhalofop-butyl.		
Parameter	Value	References
Melting point/range	45.5-49.5°C	Memo, D277695, D. Davis, 4/10/2002
pH	9.0	
Relative Density (20°C)	1.172 g/cm^3	
Water solubility (20°C)	0.44 mg/L at pH 7	
Solvent solubility (g/L)	n-heptane 6.06 n-octanol 16.0 methoanol >250 acetone >250 ethyl acetate >250 acetonitrile >250	
Vapor pressure (25°C)	5.3 x 10^{-8} kPa (4.0 x 10^{-7} mmHg)	
Octanol/water partition coefficient, Log(K_{OW}) (25°C)	3.32	

860.1200 Directions for Use

The use directions for rice and wild rice are outlined in Table 3, below.

Table 3.	**Summary of Directions for Use of Cyhalofop-butyl on Wild Rice.**					
Applic. Timing, Type, and Equip.	Formulation	Applic. Rate (lb ai/A)	Max. No. Applic. per Season	Max. Seasonal Applic. Rate (lb ai/A)	PHI (days)	Use Directions and Limitations
Rice and Wild Rice						
Broadcast foliar Ground or aerial	29.6% Emulsifiable Concentrate (Clincher SF) (2.38 lb ai/gallon)	0.19-0.28	2	0.47	60	Applications are to be made with crop oil concentrate at a rate of 2.5% v/v. A spray volume of 10-15 gallons per acre should be used. Sequential applications must be made at least 10 days apart. Do not apply through any type of irrigation system. Do not allow discharge of paddy water from treated areas for a minimum of 7 days after the most recent application.
Aerial	1.8% (wt/wt) Granular Formulation (Clincher GR)	0.19-0.28	2	0.47	60	Do not apply more than 16 lb of product per acre in a single application. Do not make more than two applications or 27.5 lbs of product per acre during a season. Sequential applications must be made at least 10 days apart. Do not allow discharge of paddy water from treated areas for a minimum of 14 days after the most recent application.

Conclusions. The use directions for rice and wild rice are adequately described and sufficient to allow evaluation of the rice residue data relative to the proposed amended tolerances. This petition makes no revisions to the label that have previously been reviewed and approved. No label changes are required in support of the amended tolerances.

860.1380 Storage Stability

The results of storage stability testing for cyhalofop-butyl, cyhalofop-acid, and cyhalofop-diacid can be found in the residue chemistry summary document prepared for rice (Memo, D267558, M. Nelson, 11/13/2001). The storage stability data are adequate to support the submitted field trial studies for cyhalofop-butyl.

860.1500 Crop Field Trials

The results of the side-by-side trials conducted with Clincher SF and Clincher GR are summarized in Tables 4 and 5. Please see Executive Summary for discussion of the use pattern associated with these trials.

Table 4. Residue Field Trial Data from Side-by-Side Crop Field Trials with Cyhalofop-butyl on Rice.

Trial ID	Formulation	Total Applic. Rate (lb ai/A)	PHI (days)	Cyhalop-acid[1] (ppm)	Cyhalofop-diacid (ppm)	Total[1] (ppm)	Avg. (ppm)
Stutgart, AK (14SRU09R-2A)	Clincher SF (NAF-541)	0.47	61	0.012, 0.012	0.257, 0.265	0.269, 0.277	0.273
	Clincher GR (GF-2112)	0.47	61	ND, ND	0.015, 0.014	0.015, 0.014	0.014 5
Winchester, AK (14SRU09R-2B)	Clincher SF (NAF-541)	0.47	59	ND, ND	[0.006], ND	[0.006], ND	<LOQ
	Clincher GR (GF-2112)	0.47	59	ND, ND	ND, ND	ND, ND	ND
East Bernard, TX (14SRU09R-2C)	Clincher SF (NAF-541)	0.47	60	ND, ND	[0.004], [0.004]	[0.004], [0.004]	<LOQ
	Clincher GR (GF-2112)	0.47	60	ND, ND	ND, ND	ND, ND	ND
East Bernard, TX (14SRU09R-2D)	Clincher SF (NAF-541)	0.47	60	ND, ND	ND, ND	ND, ND	ND
	Clincher GR (GF-2112)	0.47	60	ND, ND	ND, ND	ND, ND	ND
Sanger, CA (14SRU09R-2E)	Clincher SF (NAF-541)	0.47	61	0.011, 0.011	0.235, 0.258	0.246, 0.269	0.258
	Clincher GR (GF-2112)	0.47	61	ND, [0.008]	[0.003], [0.004]	[0.003] 0.012	0.008
Biggs, CA (14SRU09R-2F)	Clincher SF (NAF-541)	0.47	60	0.019, 0.022	0.025. 0.024	0.044, 0.046	0.045
	Clincher GR (GF-2112)	0.47	60	ND, ND	[0.003], [0.003]	[0.003], [0.003]	<LOQ

[1] Cyhalofop acid = total residue of cyhalofop-butyl and cyhalofop acid; Total = total residue of cyhalofop-butyl, cyhalofop acid, and cyhalofop diacid.

TABLE 5. Summary of Residue Data from Side-by-Side Crop Field Trials with Cyhalofop-butyl on Rice.

Formulation	Total Applic. Rate, lb ai/A	PHI (days)	Analyte[1]	Residue Levels[2] (ppm)						
				N	Min.	Max.	HAFT[3]	Median	Mean	Std. Dev.
Clincher SF (NAF-541)	0.47	59-61	Cyhalofop acid	12	ND	0.022	0.021	0.006	0.007	0.008
Clincher GR (GF-2112)	0.47	59-61	cyhalofop acid	12	ND	0.008	0.004	ND	ND	ND
Clincher SF (NAF-541)	0.47	59-61	cyhalofop diacid	12	ND	0.265	0.261	0.015	0.090	0.122
Clincher GR (GF-2112)	0.47	59-61	cyhalofop diacid	12	ND	0.015	0.015	ND	0.004	0.005
Clincher SF (NAF-541)	0.47	59-61	Total	12	ND	0.277	0.273	0.025	0.097	0.125
Clincher GR (GF-2112)	0.47	59-61	Total	12	ND	0.015	0.015	ND	0.004	0.006

[1] Cyhalofop acid = total residue of cyhalofop-butyl and cyhalofop acid; Total = total residue of cyhalofop-butyl, cyhalofop acid, and cyhalofop diacid.
[2] ND = <LOD of the method (<0.003 ppm); in calculating median, mean, and standard deviation, a value of 0 was used for ND.
[3] HAFT = Highest Average Field Trial.

Conclusions. The submitted side-by-side field trial data are acceptable and were used to support the registration of the Clincher GR formulation (Memo, D380977, W. Drew, 9/24/2010). Residues arising from use of the G formulation, Clincher GR, were significantly lower in all harvested samples (collected 59 to 61 days after the last treatment) than those found after treatment with Clincher SF, an EC formulation. An adequate number of tests were conducted on each crop in the appropriate geographical regions. All samples were analyzed for the residue of concern using an adequate method, and sample storage conditions and intervals were supported by the available storage stability data.

Given the total cyhalofop-butyl observed residues from the Clincher SF and GR trials, amended tolerances of 0.40 ppm are required for rice and wild rice, grain.

860.1550 Proposed Tolerances

The residue of concern in plants is cyhalofop-butyl, cyhalofop-acid, and cyhalofop-diacid for the purposes of risk assessment and tolerance expression. The rice tolerance is listed in 40 CFR §180.576. There are no residue chemistry data deficiencies that would preclude the establishment of a tolerance of 0.40 ppm for both rice, grain and rice, wild, grain.

For a discussion of the nature of the residue in livestock, see the earlier residue chemistry review prepared for cyhalofop-butyl (Memo, D267558, M. Nelson, 11/13/2001). In that document, the following conclusion was made: "For the purpose of this petition only, there is no reasonable expectation of finite cyhalofop-butyl residues of concern in egg, milk and edible livestock tissues [Category 3, 40 CFR §180.6(a)] as a result of the proposed uses on rice." Previously, time-

limited tolerances for rice, straw were established at 8.0 ppm. Tolerances are no longer established on rice, straw and these tolerances were allowed to expire. Rice, straw represented approximately 98% of the maximum theoretical dietary burden (MTDB) in livestock. Therefore, with the removal of rice, straw, the overall MTDB decreases substantially and the proposed amended tolerances on rice and wild rice do not result in an increase in secondary residues that are expected to occur in animal commodities. As a result, the use of cyhalofop-butyl on rice and wild rice is still considered to fall under Category 3 of 40 CFR §180.6(a) with respect to the need for cyhalofop-butyl tolerances in animal commodities.

Using the rice residue data and the OECD tolerance spreadsheet (Appendix II), the appropriate tolerance for rice, grain was calculated to be 0.4 ppm. These MRL calculations combine the residue data from the six Clincher SF trials presented here and the 18 previously reviewed residue trials for the same use pattern and formulation (Memo, D267558, M. Nelson, 11/13/2001). Of the 18 field trials previously reviewed, 15 had residues that were non-detectable or at LOQ.

No Codex, Canadian, or Mexican MRLs have been established for cyhalofop-butyl (Appendix I). As a result, the amended tolerance of 0.40 ppm tolerance to rice grain and wild rice grain will not create international MRL harmonization issues.

A tolerance summary is presented below in Table 5. It is noted that while the proposed tolerances of 0.35 ppm were calculated using the NAFTA calculator, the recommended tolerances were determined using the OECD calculator which has replaced the use of the NAFTA calculator.

Table 6. Tolerance Summary for Cyhalofop-butyl.

Commodity	Proposed Tolerance (ppm)	Existing Tolerance (ppm)	Recommended Tolerance (ppm)	Comments; *Correct Commodity Definition*
Rice, wild, grain	0.35	0.03	0.40	Proposed tolerance calculating using NAFTA calculator and recommended tolerance determined using OECD tolerance.
Rice, grain	0.35	0.03	0.40	Proposed tolerance calculating using NAFTA calculator and recommended tolerance determined using OECD tolerance.

References

PP#0F06089. NEW CHEMICAL: Cyhalofop-Butyl in/on Rice. Review of Residue Chemistry, D267558, M. Nelson, 11/13/2001

Cyhalofop-butyl: Human Health Risk Assessment for Use on Rice, D277695, D. Davis, 4/10/2002

PP# 0F06089. NEW CHEMICAL: Cyhalofop-Butyl in/on Rice, Decision Memorandum of the HED Metabolism Assessment Review Committee, D277192, Y. Donovan, 11/13/2008

Cyhalofop Butyl. Magnitude of the Residues Resulting from Food/Feed Use of the Herbicide on Rice (Supporting Section 3 Registration of a New Granular Formulation End-Use Product), D380977, W. Drew, 9/24/2010.

PP# 8E7341 Cyhalofop-butyl. Tolerance Petition for use on Wild Rice. Summary of Analytical Chemistry and Residue Data, D352156, D. Dotson, 7/7/2009.

Appendix I.
International Residue Limits

Cyhalofop-butyl (PC Code 082583; October 12, 2011)

Summary of US and International Tolerances and Maximum Residue Limits			
Residue Definition: cyhalofop-butyl, cyhalofop acid, and cyhalofop diacid			
US	Canada	Mexico[2]	Codex[3]
40 CFR 180.576: Plant: Time-limited tolerances are established for combined residues of cyhalofop (cyhalofop-butyl, R-(+)-n-butyl-2-(4(4-cyano-2-fluorophenoxy)-phenoxy)propionate, plus cyhalofop acid, R-(+)-2-(4(4-cyano-2-fluorophenoxy)-phenoxy)propionic acid) and the di-acid metabolite, (2R)-4-[4-(1-carboxyethoxy)phenoxy]-3-fluorobenzoic acid, from the application of the herbicide cyhalofop-butyl	None		None

Commodity[1]	*Tolerance (ppm) /Maximum Residue Limit (mg/kg)*			
	US	Canada	Mexico[2]	Codex
Rice, grain	0.40			
Rice, wild, grain	0.40			
Completed: Completed by M. Negussie; 10/12/2011				

[1] Includes only commodities of interest for this action. Tolerance values should be the HED recommendations and not those proposed by the applicant.

[2] Mexico adopts US tolerances and/or Codex MRLs for its export purposes.

[3] * = absent at the limit of quantitation; Po = postharvest treatment, such as treatment of stored grains. PoP = processed postharvest treated commodity, such as processing of treated stored wheat. (fat) = to be measured on the fat portion of the sample. MRLs indicated as proposed have not been finalized by the CCPR and the CAC.

Appendix II - Tolerance Assessment Calculations.

The Agency's *Guidance for Setting Pesticide Tolerances Based on Field Trial Data* was utilized for determining appropriate tolerance levels on rice and wild rice, grain. The dataset used to establish the tolerance for cyhalofop-butyl residues on rice and wild rice consisted of field trial data representing applications of the appropriate SF or GR formulations at 1x the maximum use rate. As specified by the *Guidance for Setting Pesticide Tolerances Based on Field Trial Data* SOP, the field trial application rates were within 25% of the maximum label application rate, and the PHI is consistent with the appropriate stage of maturity and the proposed PHI. The residue values used to calculate tolerance are provided in Table II-1 and the results are presented in Figures II-1.

The residue data for rice was utilized to determine the appropriate tolerance for the wild rice. The dataset for cyhalofop-butyl on rice was entered into the OECD MRL tolerance calculator spreadsheet. The calculated tolerance level for rice and wild rice, grain is 0.4 ppm (rounded MRL result).

Table II-1 Cyhalofop-butyl (input residues for Rice)

Cyhalofop-butyl
Rice
USA
GAP

Residues (mg/kg)	
0.0100	*
0.0205	
0.0100	*
0.0100	*
0.0100	*
0.0100	*
0.0190	
0.010	*
0.012	
0.010	*
0.010	*
0.010	*
0.010	*
0.010	*
0.010	*
0.010	*
0.010	*
0.010	*
0.010	*
0.273	
0.010	*
0.010	*
0.010	*
0.010	*
0.258	

Figure II-1. Data Summary Table for Cyhalofop-Butyl Residues In/On Avocado.

Cyhalofop-butyl
Rice
USA
GAP

Total number of data (n)	24
Percentage of censored data	79%
Number of non-censored data	5
Lowest residue	0.010

Highest residue	0.273
Median residue	0.010
Mean	0.032
Standard deviation (SD)	0.072
Correction factor for censoring (CF)	0.472

Proposed MRL estimate

- Highest residue	0.273
- Mean + 4 SD	0.320
- CF x 3 Mean	0.046
Unrounded MRL	0.320
Rounded MRL	**0.4**

High uncertainty of MRL estimate.
[High level of censoring]

13544

R195830

Chemical Name: Cyhalofop-butyl

PC Code: 082583
HED File Code: 11000 Chemistry Reviews
Memo Date: 11/3/2011
File ID: 00000000
Accession #: 000-00-0137

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